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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/780,438	02/09/2001	Xiaoyang Qi		7718

7590 07/02/2003

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EXAMINER
SNEDDEN, SHERIDAN

ART UNIT	PAPER NUMBER
1653	7

DATE MAILED: 07/02/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/780,438	QI, XIAOYANG	
	Examiner	Art Unit	
	Sheridan K Snedden	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 May 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-44* is/are pending in the application.

4a) Of the above claim(s) *1-15* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *16-44* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. Applicant's amendment of claims 11, 25, 37 and 42 in Paper #17, filed May 1, 2003, is acknowledged.

2. Applicant's election of invention II, claims 16-39 is acknowledged. Upon further consideration, Groups II and III are rejoined and considered. Claims 16-42 are under examination. Claims 1-15 and 43-44 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **with** traverse in Paper No. 17.

Applicant argues on page 14 and 15 of the response that a search can be conducted without any undue burden to the Examiner as the search for Group I "would include a large part of the search." This argument is not persuasive as a search for Group I would be different for both Groups II and III. Therefore, as the inventions are patentably distinct, restriction for examination purposes as indicated is proper.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 21, 26-29, and 33 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicant is also referred to the Guidelines on Written

Description published at FR 66(4) 1099-1111 (January 5, 2001) (also available at www.uspto.gov). The following passage is particularly relevant.

> The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant identifying characteristics, i.e. structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between structure and function structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. A "representative number of species" means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within a genus, one must describe a sufficient number of species to reflect the variation within the genus. What constitutes a "representative number" is an inverse function of the skill and knowledge in the art. Satisfactory disclosure of a "representative number" depends on whether one of skill in the art would recognize that applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed. In an unpredictable art, adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only one species within the genus.

Claims 21, 26-29, and 33 are directed to a composition comprising Saposin A, C or SEQ ID NO: 1-6, as well as all derivatives, homologues, fragments or analogs thereof. The specification discloses the protein of Saposin A, C or SEQ ID NO: 1-6, and general discussion regarding derivatives, homologues, fragments or analogs thereof. The specification does not provide all derivatives, fragments, analogs or naturally occurring variants, or guidance regarding how to obtain specific derivatives, fragments, analogs or naturally occurring variants that retain the function of the saposin protein.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116).

With the exception of Saposin A, C or SEQ ID NO: 1-6, the skilled artisan cannot envision the detailed chemical structure of the encompassed polypeptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only Saposin A, C or SEQ ID NO: 1-6, but not the full breadth of the claim, meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Applicant may overcome this rejection by removing from the claims the language referring to the derivatives, fragments, analogs or naturally occurring variants of saposin.

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 17-27, 29, 31, 32, 34, 37, 39, and 44 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 17-27 recites the limitation "phospholipid composition". There is insufficient antecedent basis for this limitation in the claim as the independent claim 16 recites anionic phospholipids. Applicant can overcome this rejection by amending the claim to recite "anionic phospholipids."

Claim 29 recites the limitation "phospholipid composition". There is insufficient antecedent basis for this limitation in the claim as the independent claim 28 recites anionic liposomes. Applicant can overcome this rejection by amending the claim to recite "anionic liposomes."

Claim 31 recites the limitation "wherein the concentration of liposomes". There is insufficient antecedent basis for this limitation in the claim as the independent claim 30 recites anionic liposomes. Applicant can overcome this rejection by amending the claim to recite "anionic liposomes." See also claim 39 and 44.

Claim 32 recites the limitation "wherein the biological membrane". There is insufficient antecedent basis for this limitation in the claim.

Claim 34 recites the limitation "phospholipid composition". There is insufficient antecedent basis for this limitation in the claim.

Claim 25 and 37 are indefinite as it is unclear if the composition contains all of the peptides of SEQ ID NO: 3-6 or any one of the peptides of SEQ ID NO: 3-6.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claims 40-42 are rejected under 35 U.S.C. 102(b) as being anticipated by O'Brien *et al.* (WO 9503821 A1). O'Brien *et al.* teach a Saposin C sequence that is 100% identical to SEQ ID NO: 1 and 2, which are described by the formulas of SEQ ID NO: 2-6. Thus, the reference anticipates the claimed invention.

7. Claims 16-37 and 40-44 are rejected under 35 U.S.C. 102(b) as being anticipated by Vaccaro *et al.* (IDS #30). Vaccaro *et al.* (1994) teach that Saposin C promotes the fusion of PS-liposomes in a pH-dependent manner, thereby introducing saposin C into the class of fusogenic peptides (see page 184, 2nd column). The fusogenic behavior occurred at the lower pH (regarding claims 18, 30, 38). Vaccaro *et al.* teach a liposomal composition containing Sap C and glycosylceramidase, the later of which is known for the treatment of Gaucher's disease (see Introduction, section 2.5).

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person

having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. Claims 16-25, 29-31 and 33-42 are rejected under 35 U.S.C. 103(a) as being unpatentable over Vaccaro *et al.* (IDS #30), , in view of Gross (US Patent 5,766,626), and O'Brien *et al.* (WO 9503821 A1).

Vaccaro *et al.* (1994) teach that Saposin C promotes the fusion of PS-liposomes in a pH-dependent manner, thereby introducing saposin C into the class of fusogenic peptides (see page 184, 2nd column). The fusogenic behavior occurred at the lower pH (regarding claims 18, 30, 38). Vaccaro *et al.* teach a liposomal composition containing Sap C and glycosylceramidase, the later of which is known for the treatment of Gaucher's disease (see Introduction, section 2.5).

Gross teach the use of a fusogenic peptide in conjunction with vesicle-forming lipids, at least 10% anionic phospholipid, in a composition for delivering pharmaceutical agents across a membrane. The amount of lipid was present in at least 10-fold excess, by weight to the fusogenic protein (regarding claims 17, 29, 31, 39; see column 14, lines 15-30). Gross does not teach the use of Saposin as a fusogenic peptide.

O'Brien *et al.* teach a Saposin C sequence that is 100% identical to SEQ ID NO: 1 and 2, which are described by the formulas of SEQ ID NO: 2-6 (regarding claims 23-25, 37, 40-42).

Taken together, it would have been obvious to the person of ordinary skill in the art at the time the invention was made to substitute the fusogenic peptide taught by Gross for the fusogenic peptide of Saposin taught by Vaccaro *et al.* The person of ordinary skill in the art would have be motivated to make the above substitution as Gross demonstrates the effectiveness of using a fusogenic peptide for the delivery of a pharmaceutical agent. The person of ordinary skill in the art would have expected success in making the above substitution as Vaccaro *et al.*

demonstrated the fusogenic activity of Saposin C and the conditions that favor that activity. Thus, the claimed invention was within the ordinary skill in the art to make and use at the time it was made and was as a whole, *prima facie* obvious.

10. Claims 26-28 and 43-44 are rejected under 35 U.S.C. 103(a) as being unpatentable over Vaccaro *et al.* (IDS #30), and O'Brien *et al.* (WO 9503821 A1) as applied to claims 16-21 above, and further in view of Okkels *et al.* (US Pub 2002/0127219) and Qi *et al.* (IDS #41).

Okkels *et al.* teach a method of treating Gaucher's disease, in which an effective amount of a GCB polypeptide (or acid beta-glucosidase) and a Saposin C polypeptide, or a chimeric polypeptide thereof, is administered to a patient in need thereof (see claims 19 and 57; regarding claims 43-44). The pharmaceutical composition containing the polypeptide of the invention may be administered orally, intravenously, intramuscularly, intraperitoneally, intradermally, subcutaneously, or by inhalation. The preferred mode of administration will depend upon the particular indication being treated and will be apparent to one of skill in the art (see section [0263]; regarding claims 26-28, 32). Okkels *et al.* does not teach the use of liposomal compositions as a method of delivering pharmaceutical agents.

Qi *et al.* (1998) teach that the deficiency of acid beta-glucosidase and saposin C lead to Gaucher disease (see abstract).

Taken together, it would have been obvious to the person of ordinary skill in the art at the time the invention was made to use GCB polypeptide (or acid beta-glucosidase) for the treatment of Gaucher's disease using the composition as taught by Gross and Vaccaro *et al.* above. The person of ordinary skill in the art would have been motivated and expected success to administer

acid beta-glucosidase as this is the enzyme know to be deficient in Gaucher's disease. Thus, the claimed invention was within the ordinary skill in the art to make and use at the time it was made and was as a whole, *prima facie* obvious.

Conclusion

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sheridan K Snedden whose telephone number is (703) 305-4843. The examiner can normally be reached on Monday - Friday, 8:30 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on (703) 308-2923. The fax phone number for regular communications to the organization where this application or proceeding is assigned is (703) 746-3975.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

SKS
June 30, 2003
SKS

KAREN COCHRANE CARLSON, PH.D
PRIMARY EXAMINER